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QUALITY OF LIFE OF LUNG CANCER PATIENTS IN A RANDOMIZED CLINICAL TRIAL EVALUATED BY A PSYCHOSOCIAL WELL-BEING QUESTIONNAIRE

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Abstract

The quality of life of patients treated with radiotherapy and chemotherapy for non-small cell lung cancer is compared in a randomized study. A standardized questionnaire composed of 12 questions covering psychosocial well-being (10 question index), and global quality of life evaluation (2 questions) was used to evaluate the patient's quality of life. Data were collected before treatment was started and at 7 different occasions up to 52 weeks after the beginning of the first treatment. The psychosocial well-being index and the 2 global questions were found to have a high degree of validity in a previous study. Two weeks after the start of treatment, the psychosocial well-being index for patients receiving radiotherapy was significantly higher than for patients treated by cytostatic drugs. This observation was confirmed by the 2 global questions. No differences in the quality of life were detected in the follow-up period (6–52 weeks).

Key words: Lung neoplasms; non-small cell cancer, radiotherapy, chemotherapy, randomized trial, psychosocial well-being, quality of life.

Lung cancer is one of the major causes of death among Norwegian men and an increasing death factor among women (19). The treatment on lung cancer has shown only minor progress the last few decades, except for the treatment of small cell lung cancer (1, 6, 18). Only 5 to 10% of the patients can expect to be cured by radical surgery alone (15). Non-small cell lung cancer (NSCLC) is moderately radiosensitive (13). Chemotherapy appears to have only a moderate effect. Regimens containing cisplatin have shown response rates of 20–40% with possibly some effect on survival (3, 7).

At the Norwegian Radium Hospital (NRH) a controlled clinical trial was carried out in 1983–1985 to compare the effects of radiotherapy and combination chemotherapy in patients with NSCLC. Preliminary results have shown almost identical survival rates for persons in these 2 treatment groups (7). The effect of the treatment on the patients' quality of life was also studied, a question that few clinical trials so far have dealt with. Such studies are important, particularly when only minor differences in response and survival between treatment modalities can be expected.

A generally accepted difinition of quality of life is not available (2, 5, 8). In the present study, quality of life is defined in terms of the patient's subjective evaluation of his/her life and situation. A set of questions, including a psychosocial well-being index (10 questions) and 2 global quality of life questions, was designed. In the present paper the results from this questionnaire are presented.

Material and Methods

Patient characteristics. The patients had to meet the following criteria for inclusion: previously untreated and with inoperable NSCLC, ≤70 years of age, loco-regional disease (limited disease) and good performance status (WHO 0–2). The patients were randomly assigned to combination chemotherapy or radiotherapy.

Chemotherapy consisted of:

- Day 1: Cisplatin, 70 mg/m^2, i.v. and etoposide, 100 mg/m^2, i.v.
- Days 2+3: Etoposide, 200 mg/m^2, orally.

The treatment cycles were repeated every third week with a maximum of 4 cycles. Radiotherapy consisted of mega-

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Table 1

Page one of the questionnaire. It was presented in Norwegian to the patients

	During the last fortnight would you say that you ...	Never	Occasionally	Some of the time	Often	All the time
S 1	Have felt strong and energetic?					
S 2	Have felt lonely?					
S 3	Have felt close to/intimate with another person?					
S 4	Have felt tired and rundown?					
S 5	Have felt satisfied with yourself?					
S 6	Have felt that life is worth living?					
S 7	Have been in a good mood?					
S 8	Have lacked confidence in yourself?					
S 9	Have felt depressed?					
S 10	Have felt that life is meaningless?					

voltage midline dosage of 42 Gy given in 15 fractions over 3 weeks. Treatment fields included the primary site of tumour, hilar region, mediastinal lymph nodes, and where appropriate, supraclavicular fossa. The spinal cord was shielded when the posterior field was treated in order to reduce the medulla dose to ≤ 2.6 Gy per fraction. If relapse occurred, the other treatment modality was sometimes given as a second line treatment.

Table 2

Page two of the questionnaire. It was presented in Norwegian to the patients

Taking all things together, how happy would you say you have been the last fortnight?

1. Very happy ________
2. Happy ________
3. Somewhat happy ________
4. Mixed ________
5. Somewhat unhappy ________
6. Unhappy ________
7. Very unhappy ________

Thinking about how life has been the last fortnight. Are you generally satisfied or dissatisfied?

1. Very satisfied ________
2. Satisfied ________
3. Somewhat satisfied ________
4. Mixed ________
5. Somewhat dissatisfied ________
6. Dissatisfied ________
7. Very dissatisfied ________

Design of the questionnaire. The questions used to assess the quality of life were part of a larger questionnaire that included 29 variables in the following categories: psychosocial well-being, disease and treatment related symptoms, physical function and everyday activitiy. In this paper, only the data from part S, covering psychosocial well-being and global quality of life, are reported. The psychosocial well-being questionnaire was initially composed of a 10-question scale (Table 1), and 2 global quality of life questions (Table 2). The selection of questions was based on inventories of well-being used in quality of life studies in general populations (11). The items selected were those deemed to be most suitable for a lung cancer population. Five positive and 5 negative questions were included in the index, making up 5 pairs of items covering various psychosocial dimensions (Table 1). An equal number of positive and negative questions was used to correct for the acquiescence response set, which has been found to be a problem in some quality of life studies (16). Acquiescence is the tendency of the respondent to agree with any question regardless of content. The responses to each item were scored on a 5-point scale ranging from 'not at all' to 'all the time' (giving values from 1 to 5). The global questions were scored on a 7-point scale giving values from 1 to 7. A low score represented a high quality of life.

The validity of the psychosocial well-being index and the global questions were tested in an earlier study by comparing the questionnaire results with ratings based on a semistructured interview (9). Most of the items displayed a high degree of validity. The study raised doubts concerning the validity of 3 questions (S 5 'satisfied with yourself', S 6 'feeling that life is worth living' and S 8 'lacked confidence in yourself'). These questions were, however, included in the present study in order to test

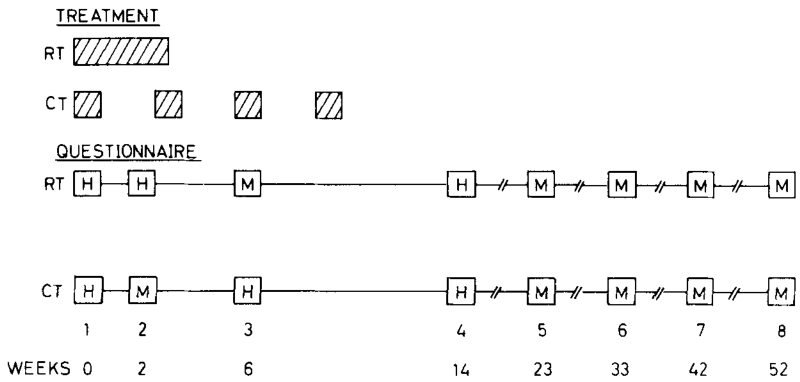

Fig. 1. Time of administration of the questionnaire and treatment. RT = radiotherapy, CT = chemotherapy, H = questionnaire answered in hospital, M = questionnaire mailed and answered at home.

Table 3

Patient characteristics

Characteristic	Radio-therapy	Chemo-therapy
No. of patients	51	44
Age (years)		
Mean	61	62
Range	37–70	47–70
Histology		
Epidermoid carcinoma	35	31
Adenocarcinoma	10	9
Large cell carcinoma	6	4
T stage		
T1	0	1
T2	16	9
T3	34	32
Tx	1	2
N stage		
N0	2	3
N1	22	16
N2	25	23
Nx	2	2
WHO performance status		
0	9	9
1	39	32
2	3	3
Weight loss during previous 3 months (mean)	3.3 kg	4.4 kg

them on a larger group of patients. Both questions for global ratings of quality of life (Table 2) were found to be valid in a previous study (9).

Study design. Before the start of treatment, all the patients were examined by a physician (SK), and they then completed the psychosocial well-being questionnaire in the hospital (Fig. 1). After 2 weeks of treatment the questionnaire was mailed to the patients in the chemotherapy group. The radiotherapy group completed it at NRH during the last part of the treatment. During the entire radiotherapy period the patients were in daily contact with the physician (SK). The third assessment took place 4 weeks later at the time of the third course of chemotherapy. The chemotherapy group completed the questions at NRH and underwent a medical examination. The radiotherapy group completed the questions at home. The fourth evaluation was undertaken 14 weeks after the initial start of treatment. At this time, all the patients had been readmitted for clinical examination. In the follow-up period, the psychosocial well-being questionnaire was mailed to patients every second month during one year or until death.

Statistical analysis. Factor analysis was made to construct an index from the 10-item psychosocial well-being questionnaire (12). This allows an assessment of the homogeneity of the answers. A small number of hypothetical variables can be extracted from a multi-item questionnaire. Factor analysis is based on the matrix of inter-item correlations. The factors extracted should account for a major part of the correlations between the original variables. The factor loadings express how strongly each of the original variables is related to the derived factors. In order to construct an index from the psychosocial well-being questions, the set of items needs to be reasonably unidimensional, i.e. a single factor should account for the major part of the correlations between the items. The factor loadings should be high for all the items included in the index; 0.40 is often used as a cutting point for the lowest accepted factor loading (17). To obtain the initial factor solution, the method of maximum likelihood was used. Separate factor analyses were undertaken at each of the observation times (1–8) (Fig. 1). The 8 analyses all yielded fairly similar results. Due to the small patient population and especially to the number of deaths that occurred in the later stages of the study, the data was subsequently pooled across all points of time and a new factor analysis performed. By using the pooled data, more stable and statistically robust results may be obtained.

In order to estimate the reliability of the psychosocial well-being scale, Cronbach's alpha was calculated (21). The alpha coefficient can be regarded as a measure of the average correlation between the items and represents a value of zero if the answers only contain random errors. If

Table 4

Compliance. Number and percentage of patients who completed the questionnaire at all times of administration

Questionnaire No.	Weeks after treatment	No. of patients: Alive	No. of patients: Completing questionnaire (percentage)
1	0	95	94 (99%)
2	2	93	84 (90%)
3	6	91	71 (78%)
4	14	77	65 (84%)
5	23	67	60 (90%)
6	33	60	48 (80%)
7	42	50	29 (75%)
8	52	40	29 (73%)

Table 5

Factor loadings. A 10-item factor analysis (for the entire scale) was carried out. Due to low factor loadings, 2 items were excluded and an 8-item factor analysis was carried out

	10-item version		8-item version	
Item	F 1	F 2	F 1	F 2
S 1	0.87	−0.34	0.86	−0.34
S 2	0.46	0.27	–	–
S 3	0.37	0.10	–	–
S 4	0.71	0.10	0.72	0.09
S 5	0.73	−0.11	0.74	−0.13
S 6	0.51	0.45	0.53	0.47
S 7	0.76	0.22	0.75	0.18
S 8	0.48	0.32	0.48	0.31
S 9	0.72	0.30	0.73	0.26
S 10	0.52	0.52	0.55	0.51
Variance	40%	10%	47%	10%

F 1 = factor one
F 2 = factor two

Table 6

Psychosocial well-being index

Questionnaire No.	Point of time	Treatment	n	Mean	SD	p value
1	Before	RT	51	2.39	0.73	
	start of treatment	CT	43	2.39	0.67	0.98
2	After 2	RT	46	2.25	0.67	
	weeks	CT	38	2.64	0.95	0.04
3	After 6	RT	38	2.25	0.60	
	weeks	CT	33	2.35	0.96	0.60
4	After 14	RT	34	2.17	0.62	
	weeks	CT	31	2.25	0.74	0.66
5	After 23	RT	31	2.30	0.66	
	weeks	CT	29	2.41	0.78	0.59
6	After 33	RT	28	2.38	0.89	
	weeks	CT	20	2.07	0.67	0.18
7	After 42	RT	19	2.18	0.69	
	weeks	CT	19	2.49	0.62	0.16
8	After 52	RT	15	2.37	0.78	
	weeks	CT	14	2.27	0.64	0.69

RT = radiotherapy, CT = chemotherapy, n = number of patients, SD = standard deviation, p = two-tailed t-test

the measures are completely reliable alpha reaches a maximum value of 1.0 A 2-tailed Student's t-test was performed to test the difference between the 2 treatment groups. In addition, analysis of covariance, using pretest scores as covariates, was performed, thereby allowing statistically more precise tests to be employed (20).

Results

Between October 1983 and December 1984, 95 new patients were included in an ongoing trial that already comprised 130 patients. Only the group of 95 received the questionnaire. The distribution of age, histology, clinical staging and WHO performance status were similar in the 2 treatment modalities (Table 3). Due to stratification for histology and the fact that the trial had been ongoing for almost 2 years, the number of patients in the 2 treatment modalities was not identical. The pre-treatment questionnaire was completed by 99% of the patients while 73% completed and mailed in the final post-treatment questionnaire after one year (Table 4). Compliance was similar for the 2 treatment modalities.

In Table 5, the factor loadings are presented. Initially, a 10-item factor analysis was carried out on all psychosocial well-being variables. Of the common variance 41% was explained by factor one. Item S 3 'have felt close to and intimate with another person', had a relatively low loading (0.37), indicating that this item should be excluded. To maintain a balance between the number of positive and negative questions posed, question S 2 'have been lonely' was also excluded. Analysis of the remaining items yielded a strong general factor accounting for 47% of the common variance, and strong factor loadings on all 8 items (>0.48). Three items, S 5, S 6, and S 8, had doubtful validity according to a previous study (9). These items had moderate to high loadings on the 8-item version (0.74, 0.53 and 0.48). It was therefore decided to include these items in the index. A composite psychosocial well-being score was constructed by computing the average score across the 8 items for each respondent. The composite score thus has the same range of variation (1–5) as the original items with a low score (1) representing the highest quality of life possible and a high score (5) representing the lowest possible quality of life. Since the validity of the 3 previously mentioned questions was uncertain, all subsequent analyses were also carried out on a 5-item index, excluding these 3 items. As the results from the 8- and 5-item analyses were practically identical, only the results from the 8-item index will be described here. In the pres-

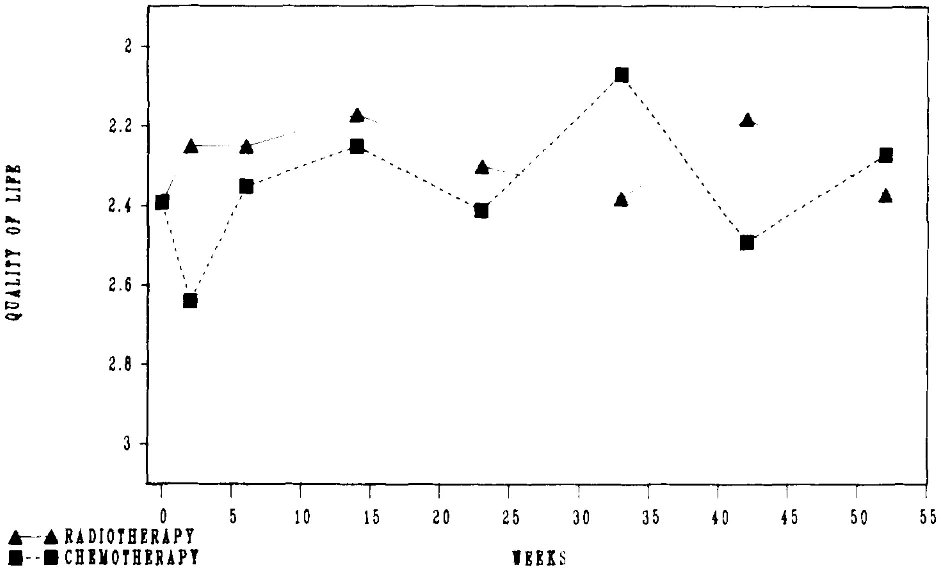

Fig. 2. Psychosocial well-being index. The mean score for the two treatment modalities are plotted. Low scores indicate a high quality of life.

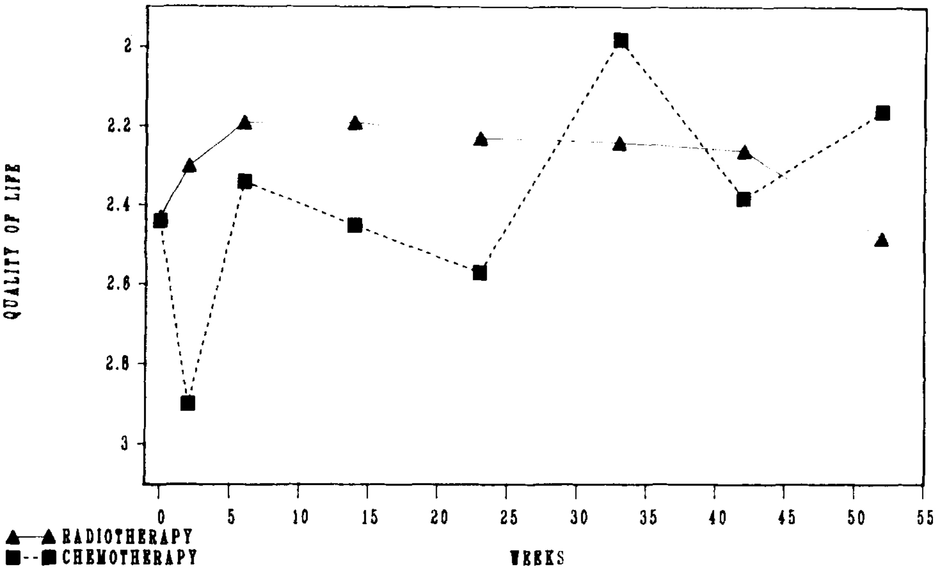

Fig. 3. Psychosocial well-being index, excluding patients with second treatments, mean scores. Low scores indicate a high quality of life.

ent analysis Cronbach's alpha was found to be highly satisfactory (0.81) for all time points.

In Table 6 and Fig. 2 the mean scores on the psychosocial well-being index for the 2 groups at every time point are presented. No difference was found in well-being before the start of treatment. After 2 weeks a statistically significant difference ($p = 0.04$) was found between the 2 treatment groups. In the radiotherapy group improvement in the quality of life was observed from the start of treatment until week 14. For the remaining study period, the number of patients was too small to provide reliable data. It should be noted, however, that the mean score of the radiotherapy group never dropped below the initial mean score. The chemotherapy patients displayed a significant drop in quality of life after 2 weeks but from 2 to 14 weeks an improvement was observed.

The use of a second treatment at relapse was optional. The radiotherapy patients were offered chemotherapy and vice versa. Fig. 3 shows the mean scores when the patients who received a second treatment modality were

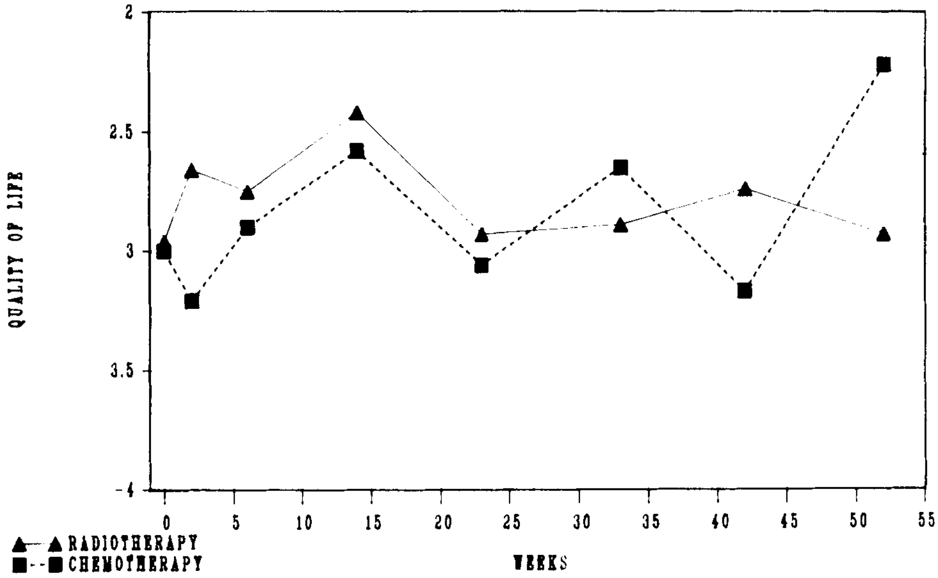

Fig. 4. Global quality of life questions, satisfaction, mean scores. Low scores indicate a high quality of life.

excluded from the analysis. Eleven patients (22%) in the radiotherapy group and 19 patients (44%) in the chemotherapy group received the second treatment. The results for the remaining patients were similar to the complete group. However, the drop in psychosocial well-being was more pronounced for the chemotherapy patients after 2 weeks and the psychosocial well-being level in the radiotherapy group after 6 weeks appears to be more stable compared to the complete group (Fig. 3).

The global quality of life questions (Table 7) generally showed the same results as the psychosocial well-being index (Figs 3 and 4). Two weeks after the start of treatment, a statistically significant difference was found between the chemotherapy and radiotherapy group for both global quality of life questions (p=0.04 and 0.02) but no major drop was seen in the chemotherapy group.

Discussion

The results showed no differences in psychosocial well-being between the 2 groups prior to treatment, as expected from the randomization. Two weeks after the start of treatment, a statistically significant difference was found in favour of radiotherapy. The results from the psychosocial well-being index and the 2 global questions concerning general happiness and satisfaction with life were similar. The group differences for the index were mainly produced by a large drop in quality of life for the chemotherapy patients but also by a slight improvement in quality of life for the radiotherapy patients. For the 2 global questions, the differences are explained by an increased quality of life for the radiotherapy patients. Except for the impaired quality of life in the chemotherapy patients after 2 weeks, a general improvement in quality of life was observed during the following 14 weeks in both treatment groups.

The available treatment for patients with inoperable NSCLC is often toxic (14). Nephro-toxicity, neuro-toxicity and myelosuppression are related to chemotherapy, while oesophagitis, dysphagia and possibly pneumonitis may be related to radiotherapy. Nausea and vomiting are common acute side-effects of chemotherapy but may also be related to radiotherapy. These symptoms are in addition often associated with a cachectic state caused by the disease itself. The differences in quality of life between the 2 groups may partly be explained by group differences in treatment related side-effects. Furthermore, the 2 treatments differ with respect to their general influence on the body. However, the chemotherapy side-effects themselves cannot be the only explanation for the decreased quality of life for the chemotherapy group at the second evaluation. If so, one would not expect an increase in quality of life at 6 and 14 weeks after start of treatment. Treatment related side-effects did not decrease during the second, third and fourth courses of chemotherapy (10). Patients may, however, have become adapted to the unpleasant effects of the cytotoxic drugs. For the radiotherapy patients a high incidence of acute side-effects (i.e. dysphagia and sore throat) were reported by the majority of the patients at 2 weeks, and this persisted at 6 weeks (10). Thus, one would have expected a decrease of the quality of life at 2 weeks for the radiotherapy patients if the side-effects had had a dramatic influence on quality of life.

What differences were there between the 2 groups during the first 2-week period in addition to treatment and

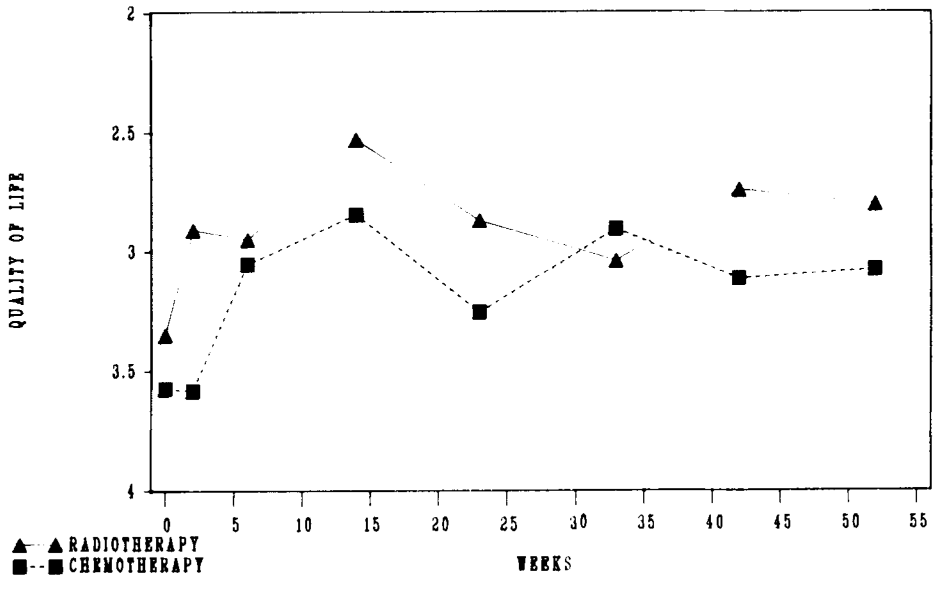

Fig. 5. Global quality of life questions, happiness, mean scores. Low scores indicate a high quality of life.

Table 7

Global psychosocial well-being

Questionnaire No.	Point of time	Treatment	n	Mean 1	Mean 2	SD 1	SD 2	p-value 1	p-value 2
1	Before start	RT	51	2.96	3.35	1.50	1.28	0.89	0.41
	of treatment	CT	44	3.0	3.57	1.33	1.27		
2	After 2	RT	47	2.66	2.91	1.18	1.25	0.04	0.02
	weeks	CT	38	3.21	3.58	1.23	1.33		
3	After 6	RT	44	2.75	2.95	1.10	1.33	0.57	0.74
	weeks	CT	39	2.90	3.05	1.27	1.32		
4	After 14	RT	35	2.42	2.53	1.36	1.18	0.58	0.32
	weeks	CT	31	2.58	2.84	1.03	1.32		
5	After 23	RT	30	2.93	2.87	1.44	1.61	0.77	0.33
	weeks	CT	28	3.06	3.25	1.17	1.38		
6	After 33	RT	28	2.89	3.04	1.64	1.84	0.55	0.76
	weeks	CT	20	2.65	2.90	1.18	1.21		
7	After 42	RT	19	2.74	2.74	1.15	1.05	0.24	0.32
	weeks	CT	18	3.17	3.11	1.04	1.18		
8	After 52	RT	15	2.93	2.80	1.58	1.66	0.53	0.64
	weeks	CT	14	2.22	3.07	1.38	1.44		

1. Satisfied/dissatisfied. 2. Happy/unhappy.
RT = radiotherapy, CT = chemotherapy, n = number of patients, SD = standard deviation, p = two tailed t-test.

side-effects? Both groups were hospitalized for the clinical examination and their first treatment. The chemotherapy patients received the cytotoxic agents and were discharged from the hospital the next day. The initial experience of chemotherapy and the resulting doubts, fears and unpleasant psychological experiences without professional help may explain the considerable drop in quality of life. In an earlier investigation it was found that the diagnosis of lung cancer often led to critical interpersonal difficulties for the patients and their families. These difficulties may have considerable impact on the patients and on the other family members' reactions to the patients (4). The patients receiving radiotherapy, on the other hand, were hospitalized for about 3 weeks. Thus, they probably received good care with continued information about disease, treatment, and medication for acute side-effects, which may have prevented negative effects on the quality of life.

After 14 weeks, all patients were hospitalized at the NRH for check-up. Patients may be optimistic during the first 14-week period. They were offered chemotherapy or radiotherapy in a highly specialized institution. Despite having cancer with a poor prognosis they received intensive treatment, and this may convey an impression of optimism on the part of the hospital. In an earlier investigation it was reported that patients treated by radiotherapy or cytotoxic chemotherapy generally considered the treatment worthwhile, whereas patients who did not receive active treatment were more likely to be depressed and dissatisfied (8).

The main evaluation of the treatment was undertaken at 14 weeks. It was the last routine check-up at the NRH. Subsequent follow-ups were made at local hospitals. The majority of the patients showed no response to the treatment at this time, and this situation may be very disappointing. However, stationary disease (no change) may, by many patients, regarded as a sign of improvement and this may be strengthened by an encouraging attitude from the staff. On the other hand, some patients have experienced progression of the disease which, combined with the stress of being discharged from the hospital responsible for the main treatment, may explain the slight drop in quality of life after the first 14 weeks. Generally, the radiotherapy patients seemed to have a higher quality of life during this period. Later in the follow-up period there was considerable fluctuation in the quality of life ratings, probably mainly due to a rapid decrease in the number of patients.

In conclusion, the questionnaire was well accepted by the patients. The method differentiated only to a limited extent between the 2 treatment modalities. Lung cancer patients reported an increase in psychosocial well-being in the first months following the start of antineoplastic treatment.

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